



Mediastinal lymph node metastases in thyroid cancer: surgery without limits

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Abstract: Metastases to lymph nodes of the superior mediastinum have been found in up to 10% of patients with thyroid carcinoma. The treatment of mediastinal lymph node metastases in thyroid cancer is still far from being standardized. However, in selected cases, especially in case of radioiodine ablation and radiation therapy failure, a surgical resection may improve the patients' survival in addition to the symptomatic benefits. We report our experience in four consecutive patients who underwent extended mediastinal surgery for large lymph node metastases from thyroid cancer during the last year. All patients were pre-operative evaluated by a multidisciplinary team involving endocrinologist, anaesthesiologist and surgeons. Surgery was carried out in all cases in two steps, firstly through a cervicotomy in order to remove the eventual local recurrence and ensure a radical neck dissection bilaterally and then by sternotomy, in order to dissect all the lymphadenopathies from the mediastinal structures. Two patients (50%) had an extended vascular infiltration and the extracorporeal circulation (ECC) and, at least, one vascular graft, were needed. No intraoperative or perioperative mortality occurred in this series. Two patients (50%) presented a sternal dehiscence that required a second surgery and a prolonged postoperative hospital stay. In all cases the surgery was radical, and the histological report revealed a macroscopic complete resection and, up to date, no recurrences were found. When feasible, surgery is more effective than systemic therapy in the treatment of thyroid cancer recurrences, especially for medullary thyroid cancer in which radioiodine therapy is ineffective and should always be evaluated in case of vascular infiltration or symptomatic patients. Moreover, due to diversity and complexity of the cervical and mediastinal structures that may be involved, a multidisciplinary medical team should always be guaranteed during the surgery.

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Introduction

Thyroid cancer is the most common endocrine malignancy and accounts for approximately 25,000 and 30,000 new cases each year in Europe and the US, respectively (1-3).

Up to 30% of patients with a thyroid cancer develops distant metastases during their lifetime and most of them by involving lymph nodes. Metastases of the superior mediastinal lymph nodes have been found in up to 10% of patients with thyroid carcinoma (4,5).

The metastatic lymphadenopathy usually arises from

the cervical region and descends along the mediastinum, behind the great mediastinal vessels. According to Sweet, most of the retrosternal lymphadenopathies are found in the antero-superior compartment of the mediastinum while, rarely are located retrotracheally or even in the posterior mediastinum (6).

The treatment of mediastinal lymph node metastases in thyroid cancer is still far from being standardized.

In advanced metastatic thyroid carcinoma, surgery has often only a palliative role in improving the symptoms (such as dysphagia, dyspnoea and obstructive sleep apnoea)

Table 1 Patients who underwent mediastinal surgery for extended lymph node metastases from thyroid cancer during the last year

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	66	47	75	68
Endocrine anamnesis	Medullary thyroid carcinoma	Medullary thyroid carcinoma	Papillary thyroid carcinoma	Solid undifferentiated thyroid carcinoma
Pre-operative chemo/radiation therapy	No	Somatostatin analogue	No	No
Surgical approach	Cervicotomy/sternotomy	Cervicotomy/sternotomy	Cervicotomy/sternotomy + extracorporeal circulation	Cervicotomy/sternotomy + extracorporeal circulation
Type of surgery	Lymphadenectomy	Thyroidectomy + Lymphadenectomy	Thyroidectomy/lymphadenectomy/left anonymous vein removal +vascular graft	Thyroidectomy/parathyroidectomy/lymphadenectomy and vascular graft
Cancer infiltration	Mediastinal/cervical lymph nodes	Cervical/mammarian/mediastinal lymph nodes	Mediastinal tissue/parietal pleura/left anonymous vein	Perithyroid tissue/ lymph nodes/superior vena cava/ Right internal jugular vein
Follow up	Alive	Alive	Alive	Alive
Post-surgical therapy	no	no	I-131	I-131
Time of surgery (min)	205	260	450	450
Complications	no	Moderate bleeding	Sternotomy dehiscence (surgery)	Sternotomy dehiscence (surgery)
Post operative stay (days)	7	6	100	55

or the syndromes (such as mediastinal mass syndrome or endocrine/paraneoplastic syndromes). However, in selected cases, especially after the systemic and radiation therapy failure, surgery may improve the patients' survival in addition to the symptomatic benefits (7-10).

We present the following cases in accordance with the CARE Guidelines.

Cases presentation

In this case series, we report our experience in four consecutive patients who underwent mediastinal surgery for extended lymph node metastases from thyroid cancer during the last year from January 2019 to July 2019), as reported in *Table 1*. All patients were pre-operative evaluated by a multidisciplinary team involving an endocrinologist, an anaesthesiologist and several surgeons of different specialities. Surgery was conducted both through a cervicotomy in order to remove the eventual local recurrence and ensure an adequate neck dissection bilaterally, and then by sternotomy to isolate all the

mediastinal structures from the lymphadenopathy. The second step was performed by a multidisciplinary surgical equipe including a thoracic, a vascular, an endocrine and a cardiac surgeon. Two patients (50%) had an extended vascular infiltration and the use of extracorporeal circulation (ECC) was needed in order to guarantee an effective vascular replacement.

Patient 1

A 66-years-old man was referred to our Department due to recurrence of medullary carcinoma in the site of the previous thyroidectomy associated to cervical and mediastinal lymph nodes metastases.

In 2016 the patient underwent total thyroidectomy for medullary micro-carcinoma with metastases to neck central compartment lymph nodes (pT1aN1Mx) associated with thyroid papillary carcinoma with multifocal follicular variant (pT1aN0M0).

During the surveillance, a chest computed tomography (CT) (*Figure 1*) reported numerous increased and

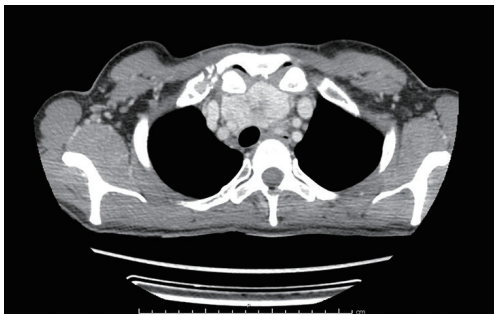


Figure 1 Pre-operative CT-scan of “patient 1”. Enlarged lymphadenopathy in the right supraclavicular region and in the superior mediastinum.

vascularized nodulations in the thyroidectomy site, the largest one in correspondence to the surgical clips and on the both sides of trachea; moreover, enlarged lymphadenopathies in the right supraclavicular region and in the superior mediastinum (left pre-vascular region and left paratracheal-paraesophageal sites) were found.

Fine-needle aspiration biopsy (FNA) of right laterocervical lymph nodes revealed cellular elements compatible with thyroid medullary cancer.

A cervicotomy followed by a longitudinal median sternotomy was performed in two steps to perform a radical laterocervical dissection and an extended macroscopic radical mediastinal lymphadenectomy by isolating both the brachiocephalic veins and the epi-aortic vessels. Post-operative hospital stay was 7 days after an eventful course. No further therapies were needed after surgery. At the time of the last-follow-up the patient was still alive and without any recurrence's signs.

Patient 2

A woman, 47-years-old; in 2013 had a laterocervical lymph node biopsy by FNA that revealed a metastasis of neuroendocrine cancer of unknown origin treated with high-dose of somatostatin analogue (lanreotide), successfully. In 2019 a thyroid check-up with ultrasound control showed intraparenchymal nodules and cervical lymphadenopathies; a second FNA revealed a thyroid medullary carcinoma. A chest CT-scan showed retrosternal large lymphadenopathy compressing left brachiocephalic vein and the cartilaginous wall of the cervical trachea together with an increased and dishomogeneous thyroid gland.

A total thyroidectomy *en bloc* with an extended cervical and mediastinal lymph nodes dissection by cervicotomy

and then median sternotomy were performed. Lymph nodes were surrounding the epi-aortic vessels for a length of 5 cm from the aortic arch, infiltrating the mammarian vessels and the sternal periosteum and compressing the left brachiocephalic vein (*Figure 2*). Histopathological examination revealed a thyroid medullary cancer with perithyroid tissues infiltration and multiple lymph nodes metastases [pT2(m)N1M1].

Post-operative hospital stay was complicated by a moderate mediastinal bleeding that required red blood cells transfusion and by a transient dysphonia that was fully recovered in one week.

Patient 3

A 75-year-old woman was admitted to our department for a cervical-mediastinal extended lesion associated with mediastinal syndrome, progressive face and neck edema and severe dysphagia.

CT-scan showed infiltration of brachiocephalic vein's junction and superior vena cava with endoluminal neoplastic thrombosis by right paratracheal lymphadenopathies, associated to an enlarged and dishomogeneous thyroid (*Figure 3*).

An endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) revealed papillary thyroid carcinoma metastases in the superior and inferior paratracheal lymph nodes. After a multidisciplinary discussion with thoracic, endocrine, cardiac and vascular surgeons, the patient underwent combined surgery.

An enlarged cervicotomy was performed by endocrine surgeon to remove macroscopically all the thyroid gland with the laterocervical lymph nodes, bilaterally. The second step was managed through a median sternotomy. The surgical equipe was consisting of a cardiac, a thoracic and a vascular surgeons who provided an extended dissection of all the lymphadenopathies from the vessels infiltrated or compressed, a left brachiocephalic vein resection and reconstruction with vascular graft, an endoluminal thrombus of the superior vena cava removal by assessing the ECC and opening the right atrium (*Figure 4*). Because an uncontrollable diffuse minimal blood leaking a mediastinal gauze packing was required, afterward sternotomy was finally closed on the post-operative day 2, in absence of bleeding. After surgery, the patient was admitted to Intensive Care Unit (ICU) for intensive monitoring. During the hospital stay, the patient developed pleural effusion and bilateral pneumonia that required a tracheotomy after

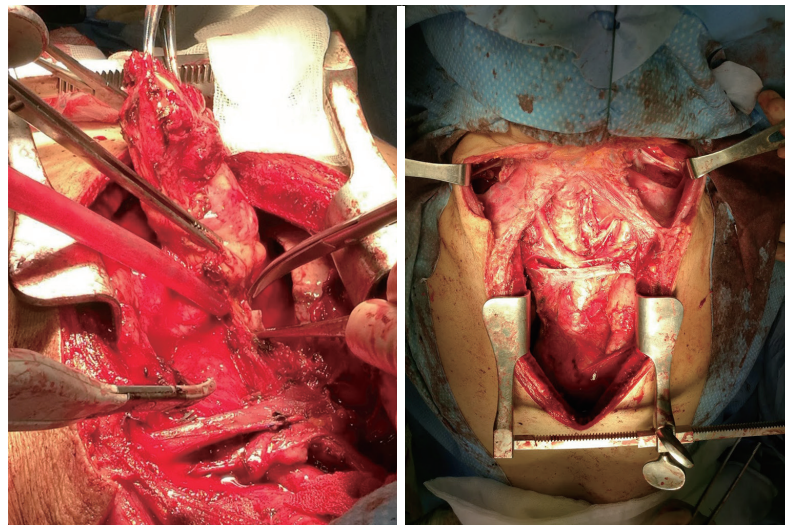


Figure 2 Intra-operative images of “patient 2”. Total thyroidectomy *en bloc* with an extended cervical and mediastinal lymph nodes dissection.



Figure 3 Pre-operative CT-scan of “patient 3”. Infiltration of brachiocephalic vein’s junction and superior vena cava with endoluminal neoplastic thrombosis by right paratracheal lymphadenopathies.

8 days to guarantee better respiratory gas exchanges and prolonged rehabilitation lasting 100 days.

Patient 4

A 68-year-old-man underwent FNA of a thyroid nodule in the right lobe and of one inferior right cervical lymph node that revealed a solid undifferentiated thyroid carcinoma.

Total body CT-scan showed the presence of neoplastic thrombosis of the right internal jugular vein, the vena cava until the right atrium (*Figure 5*) and right thyroid lobe neoplastic mass dislocating and compressing the cervical

trachea (*Figure 6*). A multidisciplinary setting consisting in an endocrine, a thoracic, a cardiac and a vascular surgeon decided for a combined surgery. A radical thyroidectomy by shaving the tracheal wall together with an extended cervical lymphadenectomy *en bloc* with external right jugular vein and superior vena cava, combined with cavo-atrial thromboarterectomy and vascular reconstruction with cadaveric and polytetrafluoroethylene (PTFE) vascular graft was performed through cervicotomy and sternotomy by using the ECC.

After surgery patient was admitted in Intensive Care Unit, and then was moved to a rehabilitation structure. After two months, for a sternal dehiscence, he was re-admitted to our department to a surgical revision.

Discussion

The mediastinum is a complex structure of the thorax that contains a wide variety of vital organs. An extended surgery in such a narrow space is often burdened by severe complications and require a high level of expertise in managing them (11). In this series no intraoperative or perioperative mortality occurred. Two patients were extubated at the end of the surgery. One patient required a tracheotomy on post-operative day 8th to ensure better respiratory exchanges while one patient was extubated after 2 days for intensive monitoring in ICU.

Two patients (50%) had a sternal dehiscence that



Figure 4 Left brachiocephalic vein reconstructed with cadaveric vascular homograft and endoluminal thrombus of the superior vena cava removal with ECC support.



Figure 5 Pre-operative CT-scan of “patient 4”. Neoplastic thrombosis of the right internal jugular vein, the cava vena until the right atrium.

required a second surgery and a prolonged (>7 days) postoperative hospital stay, nevertheless none of them developed symptoms like dyspnoea due to trachea-bronchial injury, dysphagia and cough in the post-operative course while one patient presented a dysphonia that was fully recovered in one week. These results are in line with those of other study on this matter (12,13).

In all cases we obtained a macroscopic complete resection (R0) confirmed by the histopathological examination and, up to date, no patient developed a recurrence.

Large mediastinal masses, especially those of neoplastic

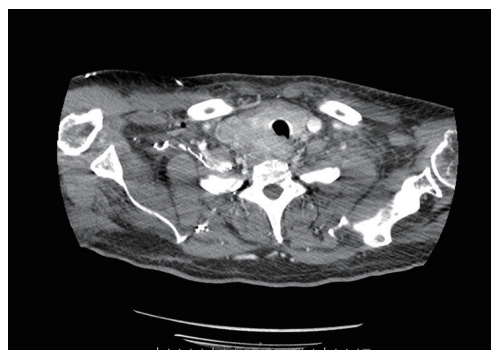


Figure 6 Right thyroid lobe neoplastic mass dislocating and compressing the cervical trachea.

nature, are frequently associated to an impaired anatomy of the surrounding structures and to the abnormal neo-vascularization. Several authors reported a less invasive approach like a partial upper sternotomy or infra-sternal approach (11,14), however in case of vascular involvement a wider surgical field should be reasonable in order to minimize the bleeding due to vascular damage. In the literature, sternotomy as surgical approach is reported in less than 5% for overall thyroidectomies performed (13,15). However, most authors support this approach in case of mediastinal node progression or when a complex dissection on the vital structures is required (16).

The role of surgery in the treatment of advanced cases of thyroid carcinoma is a topic of increasing interest thanks to the improvement of the reconstructive surgery technique and accessibility of a wide variety of prosthesis that allow a greater demolitive possibilities, even total pharynx-larynxoesophagectomy or resection of the major mediastinum vessels with a subsequent and effective reconstruction (14-16). Unfortunately, due to rarity of this kind of disease, few literatures are available on this matter, nowadays.

In this series, two patients required vascular reconstruction by graft for metastatic thrombosis. In these situations, was emblematic the essential role of a multicentric team with the help of vascular and cardiac surgeons. No complication related to the vascular graft, like dislocation. No acute bleeding complications occurred.

No complication related to ECC were found in patients who required it (nervous system complications, such as hemorrhagia, ischemia, or multi-organ failure, in particular renal failure).

In according to literature, we divided surgical cervicotomy

time by sternotomy time for better infection control (in particular to reduce risk of mediastinitis).

Patients with sternal dehiscence and prolonged intubation needed post-operative specific antibiotic drugs but no patient presented post-operative mediastinitis.

Conclusions

Surgery is more effective than systemic therapy in the treatment of thyroid cancer recurrences, especially for medullary thyroid cancer in which radioiodine therapy (I-131) is ineffective and should always be evaluated in case of vascular infiltration or symptomatic patients.

Radical dissection and a thorough reconstruction allow a long-lasting remission with good living conditions to patients unresponsive to other therapies.

Local control of the disease is the most important oncologic target of extended surgery, together with the symptomatic benefit. Regional eradication or debulking of the tumour mass, resulting in macroscopically radical surgery or in minimal residual disease, allows other therapeutic options such as with metabolic radiation, especially for distant localizations, and conventional radiation for regional oncologic sterilization.

The neck and the mediastinum are complex structures with a wide variety of vital organs. A thyroid cancer that involves both compartments requires a combined approach by involving a multidisciplinary surgical team.

In conclusion this case-series reports the effectiveness of a multidisciplinary surgery in controlling symptoms and achieve a radical resection and a good post-operative quality of life.

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